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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,906	07/14/2006	Luca Barella	4662-186	8721

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,906	BARELLA ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13 are presented for examination.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 10-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treatment of jet lag", does not reasonably provide enablement for the "**prevention** of jet lag". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method of facilitating the synchronization of circadian rhythm in humans, especially of treating or **preventing** jet lag which comprises administering to an adult person in need of such treatment or **prevention** from about 10 IU to about 1000 IU of Vitamin E per day, optionally in combination with an agent known to synchronize the circadian rhythm. The nature of the invention is extremely complex in that it encompasses the **actual prevention** of circadian rhythm disorder (i.e. jet lag) such that the subject treated with above compounds does not contract jet lag.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass prevention of a complex circadian rhythm disorder in humans which has potentially many different causes (i.e. many disease or disorders, diverse life styles). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administer the claimed compounds to a subject in order to actually **prevent** jet lag is minimal. All of the guidance provided by the specification is directed towards treatment rather than **prevention** of jet lag.

Working Examples: All of the working examples provided by the specification are directed toward the treatment rather than **prevention** of jet lag.

State of the Art: While the state of the art is relatively high with regard to treatment of circadian rhythm disorders (i.e. jet lag), the state of the art with regard to **prevention** of such disorders is underdeveloped. In particular, there

do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to **prevent** development of jet lag. The state of the art, The Merck Manual, Sixteenth Edition (1992), on page 2524, teaches that circadian dysrhythmia also known as "jet lag" can be **alleviated** by adjusting some therapeutic regimens and gradual shifts in sleeping and eating patterns. However, it is silent in terms of absolute "prevention".

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual prevention of jet lag in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of **prevention** of jet lag.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for prevention of jet lag. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard prevention of jet lag with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or

envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding prevention of jet lag with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of jet lag in a subject by administration of one of the claimed compounds.

Therefore, a method of facilitating the synchronization of circadian rhythm in humans, especially of treating or **preventing** jet lag which comprises administering to an adult person in need of such treatment or **prevention** from about 10 IU to about 1000 IU of Vitamin E per day, optionally in combination with an agent known to synchronize the circadian rhythm is not considered to be enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 provide for the use of vitamin E, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant

is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Heininger (DE19939921A1, see translated copy).

Heininger teaches a pharmaceutical composition comprising melatonin and vitamin E. Heininger teaches the pharmaceutical composition in a combination with an effective daily dose of 0.5-5mg melatonin, and 0-400mg vitamin E. (see second page). These dosages overlap and encompass Applicants dosages set forth in claim 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.,* 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kiso et al. (U.S.2003/0091614 A1).

Kiso et al. illustrates on their Fig 7, the administration of 0.005% α-tocopherol (vitamin E) enhanced effect on the circadian rhythm normalization action of melatonin. (Example 3 and Fig. 7). Kiso et al. teach that melatonin is known for a factor involved in

the regulation of the circadian rhythm. ([0009]. Kiso et al. teach that the circadian rhythm is attributed by long distance jet flights (jet lag), irregular lives due to work shifts, and desynchronisis syndrome (time zone fatigue). ([0003].

Kiso et al. do not teach the effective amounts of melatonin and vitamin E set forth in claims 13 and 10, dosing schedule set forth in claim 11, and melatonin and vitamin E in a combination to synchronize the circadian rhythm.

It would have been obvious to one of ordinary skill in the art to modify the teaching of Kiso et al. employ combination of α-tocopherol and melatonin in the single formulation for the synchronization of circadian rhythm to treat the circumstances that desynchronize the circadian rhythm because Kiso et al. teach that α-tocopherol enhances circadian rhythm normalization action of melatonin and the combination is effective as shown by their example and because long distance jet flight such as jet lags are result from the desynchronizaiton of circadian rhythm. One would have been motivated to make such a modification in order to achieve an expected enhanced benefit of normalizing circadian rhythm effectively to avoid various diseases and circumstances due to disturbance of the circadian rhythm such as jet lag. The amounts of active agents to be used, the dosing schedules are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
April 24, 2008